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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,856	03/17/2004	Stephen J. Kramer	250660US40	1969
22850	7590	03/14/2008		
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER CARTER, KENDRA D	
			ART UNIT	PAPER NUMBER
			1617	
			NOTIFICATION DATE	DELIVERY MODE
			03/14/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/801,856	Applicant(s) KRAMER ET AL.	
	Examiner KENDRA D. CARTER	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 December 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 6-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 11-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/17/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-5 and 11-14 in the reply filed on December 4, 2007 is acknowledged. The traversal is on the ground(s) that no adequate reasons and/or examples have been provided to support a conclusion of patentable distinctiveness between the identified groups. This is not found persuasive because the Examiner provided reasons and an example in the previous office action. Particularly, the groups are distinct because the product claimed can be used in a materially different process of using that product. In this case the composition of Group I can be used as a muscle relaxant or anticonvulsant.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claim 2 is objected to because of the following informalities: in line 2, the "a least one" should be "at least one". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Particularly, the specific prodrugs of zolpidem are not described in the specification, other than that the compound preferentially and/or selectively binds a α_1 receptor in the subject with a high affinity ratio of $(\alpha_1)/(\alpha_2)$ subunits in the subject (see page 10, lines 18-22). The current claim reads on compounds that may currently exist and those that have not yet been discovered, which embraces indefinite compounds.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (US 6,383,471 B1).

Chen et al. teach a pharmaceutical composition comprising a hydrophobic therapeutic agent such as zolpidem and pharmaceutically acceptable salts (see claim 11; addresses claims 1 and 2), and a carrier comprising an ionizing agent (i.e. pH buffer; see applicant's specification page 7, lines 9-10; addresses claim 3), surfactant

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(i.e. penetration agent; see column 23, line 46; column 27, line 17; applicant's specification page 7, line 3) and triglyceride (i.e. nasal carrier; see claim 1; addresses claim 1; see applicant's specification page 6, line 14). The composition can be formulated for transmucosal administration in the form of an ointment, gel, or sprayable solution (see column 35, lines 10-14 and 20; addresses claims 1 and 13). The carrier is able to solubilize the ionizable hydrophobic therapeutic agent and maintain the therapeutic agent in solubilized form for improved delivery to the absorption site (see column 4, lines 37-40). The solubilization of the therapeutic agent depends upon the therapeutic agent being ionized with the ionizing agent (see column 12, lines 51-52). Salts of the drug may be used advantageously for the sake of salt exchange with the acid or base ionizing agent, leading to better salt selection (see column 10, lines 42-26) (this claim is not being rejected). The amount of hydrophobic therapeutic agent to be used depends upon the dosage amount to be delivered. One skilled in the art can determine the appropriate dosage amount, depending upon the specific hydrophobic therapeutic agent to be delivered, the nature of the condition treat, the relative efficacy of the therapeutic agent, and other factors commonly considered (see column 10, lines 55-61). (these claims are notbeing rejected under 102(b)????) The carrier includes one or more pharmaceutically acceptable solubilizers to enhance the solubility of the drug such as water (see column 31, lines 40-44 and column 32, line 6; addresses claim 2). The amount of solubilizer is limited to a bioacceptable amounts (see column 32, lines 52-54; addresses claim 2). For compositions in the form of an aqueous dispersion, the pre-concentrate form is prepared, then the appropriate amount of purified water is

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added and the solution gently mixed (see column 35, lines 34-37). (claim 2 is not being rejected)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2, 5, 11, 12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US 6,383,471 B1) in view of Moskowitz (US 5,767,177).

Chen et al. teachings are as applied to claims 1, 3, 4 and 13 above,

Chen et al. does not specifically teach a solution of a 2:1 zolpidem/tartrate salt in sterile purified water (claim 2), or the amounts of zolpidem disclosed in claims 5, 11 and 12. Chen et al. also does not specifically teach wherein the composition is buffered to a pH of 3 to 10.

Moskowitz teaches a method of treating migraine headaches with compounds that directly or indirectly activate GABA receptors (see abstract and claim 1) such as

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zolpidem in 100 μ g/kg (see claim 7 and column 13, line 23) or between 0.01 mg/kg to 2000 mg/kg per day (see column 10, line 11).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Chen et al. and a 2:1 zolpidem/tartrate salt in sterile purified water as disclosed in claim 2 because of the following teachings of Chen et al.: 1) the pharmaceutical composition comprises a hydrophobic therapeutic agent such as zolpidem and pharmaceutically acceptable salts (see claim 11); 2) salts of the drug may be used advantageously for the sake of salt exchange with the acid or base ionizing agent, leading to better salt selection (see column 10, lines 42-26); 3) the carrier includes on or more pharmaceutically acceptable solubilizers to enhance the solubility of the drug such as water (see column 31, lines 40-44 and column 32, line 6); 4) for compositions in the form of an aqueous dispersion, the pre-concentrate form is prepared, then the appropriate amount of purified water is added and the solution gently mixed (see column 35, lines 34-37); and 5) the amount of solubilizer is limited to a bioacceptable amounts (see column 32, lines 52-54). Thus one skilled in the art would be able to formulate the salt formation of the drug and the ratio because it is advantageous to the composition in regards to solubization and what is bioacceptable to the patient.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Chen et al. and the amounts of

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zolpidem disclosed in claims 5, 11 and 12 because of the following teachings: 1) Chen et al. teach the amount of the hydrophobic therapeutic agent to be used depends upon the dosage amount to be delivered and that one skilled in the art can determine the appropriate dosage amount, depending upon the specific hydrophobic therapeutic agent to be delivered, the nature of the condition treat, the relative efficacy of the therapeutic agent, and other factors commonly considered (see column 10, lines 55-61); 2) Moskowitz teaches a method of treating migraine headaches with zolpidem in 100 $\mu\text{g/kg}$ (see claim 7 and column 13, line 23) or between 0.01 mg/kg to 2000 mg/kg per day (see column 10, line 11); and 3) it is the normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages. See In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980) (“[D]iscovery of an optimum value of the result effective variable in a known process is ordinarily within the skill of the art.” See, e.g., In re Baird, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). *In re Paterson* Appeal No. 02-1189 (Fed. Cir. January 8, 2003). Thus, one skilled in the art would be able to determine the appropriate amount of zolpidem to comprise in the composition based on the information provided above.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Chen et al. and wherein the composition is buffered to a pH of 3 to 10 (claim 14) because Chen et al. teach that the

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composition comprises an ionizing agent (i.e. pH buffer; see applicant's specification page 7, lines 9-10), in which the solubilization of the therapeutic agent depends upon the therapeutic agent being ionized with the ionizing agent (see column 12, lines 51-52). Thus, upon ionization of zolpidem, the composition will obviously be between the pH of 3 to 10 in order to be solubilized. Particularly, the ionization of zolpidem will result in a basic solution in order to be solubilized, which can fall within the pH range of 8-10.

Conclusion

No claims allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/K. D. C./
Examiner, Art Unit 1617

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617